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Syndecans-1 and -4 are induced during wound repair of neonatal but not fetal skin.

Gallo R, Kim C, Kokenyesi R, Adzick NS, Bernfield M.

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Syndecans are a family of four cell surface proteoglycans that bind to various components of the extracellular environment and can regulate many cellular behaviors including growth, adhesion, and movement. To determine whether syndecans can function during wound repair, we have examined expression of the syndecans during wound repair of adult mouse and neonatal or fetal human skin. Syndecan-1 and -4 were induced in the dermis within 12 h after incisional injury of murine or neonatal human skin. Syndecan-1 was induced primarily on endothelium, and syndecan-4 was present throughout the dermis at the site of injury. Following re-epithelialization, expression of the syndecans return to their baseline level. In marked contrast to these observations, wounded human fetal skin showed no increase in expression of syndecans. This lack of increase in the expression of syndecans by cells of the dermis correlates with prior observations that fetal skin heals without a polymorphonuclear cell infiltrate, appreciable fibrosis, or clinically apparent scar. Thus, induced expression of syndecans is not an absolute requirement for wound repair but does correlate with the occurrence of fibrosis in mature skin. These findings support the role of syndecans as regulators of cell behavior and suggest that syndecan-1 and -4 induction in the dermis may contribute to events that lead to inflammation and fibrosis.

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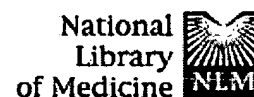
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Syndecan-4 deficiency impairs the fetal vessels in the placental labyrinth.

Ishiguro K, Kadomatsu K, Kojima T, Muramatsu H, Nakamura E, Ito M, Nagasaka T, Kobayashi H, Kusugami K, Saito H, Muramatsu T.

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Syndecan-4 is a transmembrane protein bearing heparan sulfate chains, involved in anticoagulation and focal adhesion formation. Here, we revealed that syndecan-4 was expressed in the fetal vessels in the placental labyrinth by in situ hybridization and immunohistochemical staining. At 17.5 gestational days, the area of degenerated fetal vessels in the placental labyrinth was more diffuse and larger in Synd4(-/-) embryos than wild-type controls. Calcium and fibrin(ogen) depositions in the degenerated vessels were also more extensive and more severe in the placentas of Synd4(-/-) embryos. These findings suggest that syndecan-4 deficiency impairs the fetal vessels in the placenta, probably due to a deficit in the anticoagulation mechanism. This article is the first report demonstrating that among a large number of core proteins of heparan sulfate proteoglycans, a defect of a single core protein caused impaired anticoagulation in a specific site. Copyright 2000 Wiley-Liss, Inc.

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ARTICLES

Induced expression of syndecan in healing wounds

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We have studied the expression of an integral cell surface proteoglycan, syndecan, during the healing of cutaneous wounds, using immunohistochemical and in situ hybridization methods. In normal mouse skin, both syndecan antigen and mRNA were found to be expressed exclusively by epidermal and hair follicle cells. After incision and subsequent suturing, remarkably increased amounts of syndecan on the cell surfaces of migrating and proliferating epidermal cells and on hair follicle cells adjacent to wound margins were noted. This increased syndecan expression was shown to be a consequence of greater amounts of syndecan mRNA. Induction was observed already 1 d after wounding, was most significant at the time of intense cell proliferation, and was still observable 14 d after incision. The migrating cells of the leading edge of the epithelium also showed enhanced syndecan expression, although clearly less than that seen in the proliferating epithelium. The merging epithelial cells at the site of incision showed little or no syndecan expression; increased syndecan expression, however, was detected during later epithelial stratification. When wounds were left unsutured, in situ hybridization experiments also revealed scattered syndecan-positive signals in the granulation tissue near the migrating epidermal sheet. By immunohistochemical analysis, positive staining in granulation tissue was observed around vascular endothelial cells in a subpopulation of growing capillaries. Induction of syndecan in granulation tissue both at the protein and mRNA levels was temporally and spatially highly restricted. Granulation tissue, which formed in viscose cellulose sponge cylinders placed under the skin of rats, was also found to produce 3.4 and 2.6 kb mRNA species of syndecan similar to that observed in the normal murine mammary epithelial cell line, NMuMG. These results suggest that syndecan may have a unique and important role as a cell adhesion and a growth factor-binding molecule not only during embryogenesis but also during tissue regeneration in mature tissues.

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